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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/767,597	01/22/2001	Timothy J. Jegla	018512-002211US	2516

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EXAMINER	
CHERNYSHEV, OLGA N	
ART UNIT	**PAPER NUMBER**
1646	9

DATE MAILED: 11/04/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/767,597	JEGLA, TIMOTHY J.	
	Examiner	Art Unit	
	Olga N. Chernyshev	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *13, 15-18* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Response to Amendment

1. The claims 14 and 19 have been cancelled and claim 13 has been amended as requested in the amendment of Paper No. 8, filed on August 13, 2002. Claims 13 and 15-18 are pending in the instant application.

2. The Text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action

3. Any objection or rejection of record, which is not expressly repeated in this action has been overcome by Applicant's response and withdrawn.

4. Applicant's arguments filed on August 13, 2002 have been fully considered but they are not deemed to be persuasive.

Claim Rejections - 35 USC § 101

5. Claims 13 and 15-18 stand rejected under 35 U.S.C. 101 because the claimed invention is drawn to an invention with no apparent or disclosed specific and substantial credible utility for the reasons of record as applied to claims 13-19 in section 2 of paper No. 6. Briefly, the instant application has provided a description of an isolated nucleic acid encoding a polypeptide and the polypeptide encoded thereby. The instant application does not disclose the biological role of this polypeptide or its significance.

Applicant traverses the rejection on the premises that the substantial and specific credible practical utility of the novel human Hac3 polypeptides as novel cation channels lies in the fieled of development of agonists and antagonists of Hac3 channels, which "are useful for modulating

cell excitability and in controlling CNS diseases related to cell excitability" (page 3, last paragraph and page 4, first paragraph of the Response). Applicant urges to the Declaration of Dr. Neil Castle to support such statement of utility of Hac3. Applicant further continues that because Hac3 channel is "a hyperpolarized activated cation channel that is widely expressed in the central nervous system" (page 5, third paragraph of the Response), and is, therefore, capable of modulating cell excitability, "the Hac3 channel is a useful target for the treatment of diseases and conditions caused by altered neuronal and cell excitability in the CNS" (page 6, first paragraph). Thus, Applicant asserts a specific utility for Hac3 molecules as "identification of Hac3 channels that influence cell excitability in the CNS" (page 8, last paragraph); substantial utility as "identification of agonists or antagonists of Hac3 channels useful for treating diseases of hyperexcitability" (page 9, first paragraph), and credible utility as that "one skilled in the art, after reading this application, would (a) know how to identify Hac3 channels (b) know how to identify agonists or antagonists of Hac3 channels (c) know how to use these agonists or antagonists to modulate cell excitability" (page 9, second paragraph). These arguments have not been found to be persuasive for the following reasons.

It was never disputed or doubted that the claimed novel Hac3 polypeptides can be hyperpolarized activated cation channels. As it is well known in the art, each cell expresses and produces a number of ion channels. It is also known from the literature, that cation channels are involved in a broad range of functions, rhythmic activity of the cells and changes in membrane potentials among them. However, the instant specification fails to describe what is the practical utility of the claimed invention. There is no evidence of the record showing that the new cloned cation channel is associated with any specific physiological function. Nor is it shown that it is

associated with known compounds, specific effects or known disorders or diseases. Therefore, in the absence of knowledge of the biological significance of this specific polypeptide, there is no immediately obvious patentable use for it.

One skilled in the art would not reasonably believe or find it credible that administration of modulators of Hac3 polypeptides would have an effect or make a difference in treatment of such a broad range of unrelated disorders as "various pacemaker dysfunctions such as familial sinus rhythm diseases, sick sinus syndrome associated with atrial fibrillation, sinus tachycardias and bradycardias as well as ventricular arryhythmias. [...] [M]emory and learning disorders, sleeping disorders, bipolar disease, schizophrenia, CNS disorders such as migraines, hearing and vision problems, seizures, and neuroprotective agents (e.g., to prevent stroke)" (page 9 of the instant specification, lines 2-8). Moreover, the instant specification fails to provide any evidence or sound scientific reasoning that hyperpolarized activated cation channel Hac3 is specifically associated with all these diseases and conditions. It would require making significant inventive contribution for one skilled in the art to discover which one of the disease or conditions stated in the instant specification can be treated by administration of agonist or antagonist of Hac3 polypeptide. Therefore, one would reasonably conclude that at the time the invention was made, no specific and credible utility for the claimed Hac3 polypeptides was disclosed.

The fact that HAC3 is expressed in different tissues still does not identify the substantial, specific or credible utility because one skilled in the art would not know how to use the novel HAC3 channel in practical application. Yet, the characterization and discovering the biological significance and function of the claimed protein is part of the act of invention.

The Declaration of Dr. Neil Castle under 37 CFR 1.132 filed on August 13, 2002 has been carefully considered but found to be insufficient to overcome the rejection of claims13 and 15-18 based upon lack of practical utility as set forth in the last Office action. The Declaration provides support for assertion of utility of Hac3 polypeptides as hyperpolarization-gated cation channels "in promoting neuronal excitability" and, therefore, being useful "for the treatment of diseases of hyperexcitability, such as epilepsy and migraine" (see page 3, sections 7 and 8 of the Declaration). However, according to the instant specification at the time the invention was made, Hac3 polypeptides were asserted to be associated with multitude of unrelated disorders and medical conditions, which stands for broad, unspecified and non credible utility. Subsequent discovery that modulators of Hac3 channels can be useful in treatment of epilepsy and migraine provides for specific and substantial utility of Hac3; nevertheless, Applicant cannot relay upon later findings to support assertion of specific utility. Thus, according to the instant specification, at the time of invention the biological function of Hac3 was not disclosed, and no information about specific and credible utility for Hac3 was provided.

Claim Rejections - 35 USC § 112

6. Claims 13 and 15-18 stand rejected under 35 U.S.C. 112, first paragraph for the reasons of record in section 3 of Paper No. 6. Briefly, because the claimed invention is not supported by either a clear asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

7. Claims 13 and 16-18 stand rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably

convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention for those reasons of record as applied to claims 13-19 in section 4 of Paper No. 6.

Applicant argues that "[t]he claims fully comply with the requirements for written description of a chemical compound of a chemical genus as set forth in *University of California v. Eli Lilly & Co.*" (page 10, last paragraph of the Response). Applicant also submits that the instant specification fully discloses a polypeptide of SEQ ID NO: 1, and "[t]he polypeptides are claimed by reference to shared structural features, *i.e.*, percent identity to the sequence disclosed in SEQ ID NO: 1" [and shared] "functional features, *i.e.*, the ability to form a cation channel having the characteristic of activation upon hyperpolarization" (page 11, second paragraph). The Examiner maintains the position that claims 13 and 16-18 do not satisfy the written description requirements for the following main reasons.

The instant specification fails to describe the entire genus of proteins which are encompassed by "an isolated polypeptide [...] having an amino acid sequence that has greater than 96% identity to SEQ ID NO: 1" (claim 13). There is no reference that would direct one skilled in the art to a predictability of structure of those polypeptides that have sequence identity of 96% or more to SEQ ID NO: 1 and maintain the desirable function of a cation channel because there is only a single example of SEQ ID NO: 1 provided in the specification and because there is no guidance can be found in the prior art. Also, the instant application fails to recite relevant identifying physical and/or chemical and/or functional characteristics coupled with a known or disclosed correlation between function and structure that are sufficient to describe the claimed invention in such full, clear, concise and exact terms that a skilled artisan

would recognize applicant was in possession of the claimed invention. In addition, there is no reference to a representative number of species for the claimed genus or disclosure of a molecular embodiment that lacks SEQ ID NO: 1 and still possess the function of a cation channel.

Applicant's argument that "a sequence that diverges even by only one amino acid is not a species of Hac3 if it doesn't form a cation channel when expressed" (page 12, first paragraph) contradicts the subject matter that is claimed in claim 13. Claim 13 encompasses a polypeptide of more than 96% sequence identity to SEQ ID NO: 1, which constitutes more than one amino acid substitution, and forms a cation channel. Thus, there is a clear lack of written description in the instant specification of the polypeptides that have greater than 96% identity to SEQ ID NO: 1 if, according to Applicant's own statement, there are sequences that have 96% identity to SEQ ID NO: 1 and do not "form a cation channel when expressed".

Conclusion

8. No claim is allowed.

9. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37

CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Olga N. Chernyshev whose telephone number is (703) 305-1003. The examiner can normally be reached on Monday to Friday 9 AM to 5 PM ET.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached on (703) 308-6564. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 782-9306 for regular communications and (703) 782-9307 for After Final communications.

Certain papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax center located in Crystal Mall 1 (CM1). The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)0. NOTE: If Applicant *does* submit a paper by fax, the original signed copy should be retained by Applicant or Applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers.

Official papers filed by fax should be directed to (703) 308-4556 or (703) 308-4242. If either of these numbers is out of service, please call the Group receptionist for an alternative number. Faxed draft or informal communications with the examiner should be directed to (703) 308-0294. Official papers should NOT be faxed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Olga N. Chernyshev, Ph.D. OC
November 1, 2002

JOHN ULM
PRIMARY EXAMINER
GROUP 1600